REMARKS

The present invention relates to novel cancer vaccines. More particularly, the invention relates using hapten-modified syngeneic tumor cells to elicit anti-tumor T cell responses in a cancer patient thereby providing a therapeutic benefit.

The above-captioned application is a divisional application of U.S. Patent Application No. 09/134,465, filed August 14, 1998 (the "parent application"), now issued as U.S. Patent No. 6,333,028, which is a continuation-in-part of U.S. Patent Application No. 08/899,905, filed July 24, 1997, now abandoned.

This application was filed to prosecute an invention that was not elected in the parent application. Accordingly, in Response to Restriction Requirement mailed April 9, 2003 (Paper No. 6), Applicant elected claims 1, 2, and 4-8 for examination. Applicant has herein canceled claims 1, 4, and 5, consistent with the species election required by the Examiner. Claims 9-21 stand withdrawn from further consideration as drawn to non-elected inventions. Claims 2, and 6-7, have now been amended and new claims 22-24 have been added. No new matter has been added by way of these new claims or amendments as more fully set forth below. Thus, claims 2, 6-8, and 22-24, are under consideration in the present application.

Election of Species

By Response filed July 8, 2003 (Paper No. 8), in response to Restriction Requirement mailed April 9, 2003 (Paper No. 6), Applicant elected the claims of Group I, claims 1, 2, and 4-8, for examination in the present application. Applicant, by telephonic election (Interview Summary of August 26, 2003; Paper No. 10), further elected the species of dinitrophenyl ("DNP") as the hapten. Applicant hereby affirms the election of DNP.

Further, also by telephone interview (*see* Paper No. 10), the Examiner requested that Applicant elect between an ovarian carcinoma and a colon carcinoma, both recited in claim 2. Applicant elected colon carcinoma by telephone, and this election is hereby confirmed.

Specification

The Examiner has requested that the specification, at page 1, be amended to reflect the status of the parent applications. Accordingly, the specification has been amended, at

page 1, to set forth the status of the related applications. More particularly, the specification, as now amended, reflects that the present application is a divisional application of patent application No. 09/134,465, filed August 14, 1998, now issued as U.S. Patent No. 6,333,028, which is a continuation-in-part of U.S. Patent Application No. 08/899,905, filed on July 24, 1997, now abandoned.

The amendment adds no new matter, but serves to set forth the proper relationship between the above-captioned application and related applications as well as to reflect the status of the parent applications.

Rejection of claims 1, 2, and 4-8 under Doctrine of Obviousness-type Double Patenting

Claims 1, 2, and 4-8, stand rejected pursuant to the doctrine of obviousness-type double patenting. In the Examiner's opinion, the claims are unpatentable over claims 1-4 of the '028 patent because the claims of the instant application are generic to the patented claims in that the instant claims read on a method of treating an adenocarcinoma, wherein the tumor cells are autologous, wherein the hapten is DNP, and wherein the composition comprises an immunological adjuvant, *e.g.*, Bacille Calmette-Guerin ("BCG").

Applicant, while respectfully disagreeing with the Examiner's reasoning, has canceled claims 1, 4, and 5, in accordance with the restriction/species requirements in the instant application, and has amended, *inter alia*, claim 2, from which the remaining claims depend, consistent with the species elections of August 26, 2003 (Interview Summary, Paper No. 10), solely to expedite prosecution. Claim 7 has been amended to now depend from claim 2. Thus, the claims as amended in the present application recite that the adenocarcinoma is a colon carcinoma, while the claims of the '028 patent recite an ovarian carcinoma. This amendment adds no new matter, but serves merely to re-write claim 2 in independent form now that claim 1, from which claim 2 depended previously, has been canceled, and to comport with the various species elections required in the instant application.

Applicant respectfully points out that in the Examiner's view, these two adenocarcinomas (*i.e.*, colon and ovarian) are patentably distinct from each other such that a species election was required. Accordingly, claim 2, as amended herein to recite that the adenocarcinoma is a colon carcinoma, cannot read on the claims of the '028 patent, which are drawn to methods relating to ovarian carcinoma, for purposes of obviousness-type double

patenting. Therefore, the claims as amended cannot read on the claims of the parent application, and the rejection for double patenting is now moot. Thus, Applicant respectfully requests reconsideration and withdrawal the rejection of claims 2, and 6-8 (claims 1, 4, and 5, having been cancelled) under the doctrine of obviousness-type double patenting.

Moreover, in the event that claims 2 and 6-8, as amended, somehow are viewed to read on the claims of the '028 patent, Applicant, in a good faith effort to expedite prosecution of this application, hereby agrees to file a Terminal Disclaimer as to claims 2, and 6-8 of the instant application upon notice that these claims contain allowable subject matter.

Rejection of claim 1, 2, and 4-8 under 35 U.S.C. §112, first paragraph - enablement

The Examiner has rejected claims 1, 2, and 4-8, pursuant to 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner is of the opinion that while the specification is enabling for a method for treating adenocarcinoma/colon carcinoma comprising administering autologous irradiated colon carcinoma cells, the specification does not provide enablement for administering syngeneic cells.

Applicant, while respectfully not agreeing with the Examiner's reasoning, in a good faith effort to expedite prosecution of this application, has amended claim 2 (claim 1 having been canceled to conform with election of species) to recite autologous. Further, Applicant has now canceled claim 4 since the subject matter recited therein is now recited in claim 2, as amended. Therefore, Applicant respectfully requests that the rejection of claims 2, and 6-8 (claims 1, 4 and 5 having been canceled herein) under 35 U.S.C. §112, first paragraph, is now moot and should be reconsidered and withdrawn.

Rejection of claim 1, 2, and 4-8 under 35 U.S.C. §112, first paragraph - enablement

Claims 1, 2, and 4-8, stand rejected pursuant to 35 U.S.C. §112, first paragraph, for lack of enablement. More specifically, the Examiner is of the opinion that the specification is enabling for a method of treating adenocarcinoma/colon carcinoma, comprising administering autologous irradiated colon carcinoma cells, but does not provide enablement for administering human tumor cells "substantially in a no growth phase." The Examiner contends that this term reads on cells that are still able to grown and divide, thereby requiring undue experimentation to practice the invention commensurate with the scope of the claims. Applicant respectfully

submits that claims reciting cells "substantially in a no growth state", as amended claim 2 now recites, are amply enabled by the specification as filed for the reasons set forth below.

Preliminarily, claims 1, 4 and 5, have been canceled herein, rendering any rejection of these claims now moot.

It is well-settled that applicant need not have actually reduced the invention to practice prior to filing in order to satisfy the enablement requirement under 35 U.S.C. §112, first paragraph. MPEP §2164.02 (citing *Gould v. Quigg*, 822 F.2d 1074 (Fed. Cir. 1987)). Indeed, the invention need not contain a single example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation (*In re Borkowski*, 422 F.2d at 908), and "representative samples are not required by the statute and are not an end in themselves" (*In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970)). Thus, 35 U.S.C. § 112, first paragraph, enablement does not require any working examples under the current patent law.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. MPEP §2164.01 (citing *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976)). The fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. *Id.* Further, the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. MPEP §2164.05(a) (citing *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991)). Therefore, under current law, enablement does not require a working example and experimentation is allowed so long as it is not undue, where the inquiry as to what is undue is framed within the context of the level of experimentation performed in the relevant art.

Under the present patent law, claims 2, and 6-8, are enabled under 35 U.S.C. §112, first paragraph. More specifically, the specification makes clear that "substantially in a state of no growth" refers to cells "which are not going to grow and divide after administration into the subject" such that they are "cells that will not divide *in vivo*." Specification as filed at page 10, lines 17-20. Further, the specification notes that methods for suspending cells in a state of no growth were well-known in the art. *Id.* at lines 21-24. Moreover, the specification points out that there was extensive knowledge in the art relating to producing tumor cells for use in a vaccine where the tumor cells did not grow when administered to a human:

> It is theoretically possible that injected tumor cells could grow in a patient's skin. However, this has not been observed in more than 200 patients injected with vaccines, prepared similarly to the vaccine of the present invention, to various cancers to date and is considered a very remote possibility.

Specification at page 21, lines 1-5. Thus, methods of providing tumor cells to a patient where the cells were "substantially in a no growth state", that is, where the tumor cells did not grow and divide when administered to a patient, were known in the art. Therefore, even assuming, *arguendo*, that experimentation would be required to produce tumor cells that were "substantially in a no growth state," as amended claim 2 now recites, the art routinely carried out such experimentation. Furthermore, the data disclosed in the specification as filed also demonstrate that the tumor cells of the invention, when administered to a patient, did not grow and divide and were, therefore, substantially in a no growth state. Applicant respectfully submits that the skilled artisan, based upon the disclosure provided in the specification as filed and the high degree of skill in the art, would not have required any undue experimentation to produce the cells of the invention, including cells "substantially in a no growth state" as defined and exemplified in the specification.

For the reasons stated above, claims 2, and 6-8, as amended, are supported by the specification as filed and are enabled under 35 U.S.C. §112, first paragraph. Therefore, Applicant respectfully requests that the rejection of claims 2, and 6-8, pursuant to 35 U.S.C. §112, first paragraph, for lack of enablement, be reconsidered and withdrawn.

Rejection of claim 1, 2, and 4-8 under 35 U.S.C. §112, first paragraph - enablement

Claims 2, and 6-8, stand rejected (claims 1, 4, and 5 having been canceled) pursuant to 35 U.S.C. §112, first paragraph, for lack of enablement. More specifically, the Examiner reasons that while enabling for a method of treating an adenocarcinoma/colon cancer in a human patient comprising administering the haptenized syngeneic colon cancer cells and Bacille Calmette-Guerin (BCG), the specification does not support such treatment without administering BCG. In support of this rejection, the Examiner cites Hoover et al. (1985, Cancer 55:1236-1243) and U.S. Patent No. 5,290,551, to Applicant. Applicant respectfully submits that

the claims of the invention reciting "an adjuvant" are not limited to BCG and that claims 2, and 6-8, are enabled as to other adjuvants.

Applicant respectfully points out that Hoover and the '551 patent merely teach that BCG is an adjuvant that can be used, but these references do not teach that only BCG can be used as adjuvant, especially with respect to the present invention which does not relate to the cells used either in Hoover or in the '551 patent. Further, the specification discusses additional adjuvants that, without being limited to only those adjuvants, can be used in the methods of the invention (*e.g.*, specification as filed at page 13, lines 5-10) (discussing various adjuvants, *inter alia*, BCG, QS-21, and interleukin 12). Applicant respectfully submits that because adjuvants in general, including BCG, are amply supported by the specification as filed, and because the teachings of Hoover or the '551 do not suggest or indicate that only BCG can be used as an adjuvant, this rejection should be reconsidered and withdrawn.

Additionally, no undue experimentation is required where, even if experimentation is needed to practice the methods of the invention using other adjuvants, the art typically engaged in such experimentation. Thus, where the art typically engaged in experimentation to optimize a vaccine by selecting from various adjuvants, *e.g.*, BCG, QS-21, and the like, such experimentation would not be undue for purposes of Section 112, paragraph one, enablement. Accordingly, the claimed invention is not limited to only BCG, and other adjuvants are enabled as would have been readily appreciated by the skilled artisan, based upon the disclosure provided in the specification as filed.

Applicant respectfully submits that other adjuvants, including, but not limited to, BCG, QS-21 and IL-12, are amply supported by the specification and the invention should not be limited to BCG. Therefore, Applicant respectfully contends that claims 2, and 6-8, are amply enabled under 35 U.S.C. §112, first paragraph, and the rejection of these claims should be reconsidered and withdrawn.

Rejection of claims 1, 2, and 4-8 under 35 U.S.C. §112, second paragraph

Claims 2, 6-8 (claims 1, 4, and 5, having been canceled herein) stand rejected pursuant to 35 U.S.C. §112, for being, in the Examiner's opinion, indefinite for reciting the term "tumor cell substantially in a no growth phase." Applicant respectfully submits that the claims are not indefinite in any way.

Nonetheless, while respectfully not agreeing with the Examiner's reasoning, Applicant, in a good faith effort to expedite prosecution of this application, has amended claim 2, from which the remaining claims depend, to recite the term "state" instead of "phase." Applicant respectfully submits that the claims, as amended, are not indefinite in any way as more fully discussed below.

It is settled law that the "patent law allows the inventor to be his own lexicographer." *Chicago Steel Foundry Co. v. Burnside Steel Foundry Co.*, 132 F.2d 812 (7th Cir. 1943). *See also* MPEP §2173.01. This is because "[t]he dictionary does not always keep abreast of the inventor. It cannot. Things are not made for the sake of words, but words for things." *Autogiro Co. v. U.S.*, 155 USPQ 697 (Ct. Cls. 1967). Further, applicant is entitled to have the claims construed in connection with the other parts of the application. *See Autogiro Co. v. U.S.*, 155 USPQ 697 (Ct. Cls. 1967). Moreover, where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings"). Therefore, Applicant is entitled to define terms to describe his invention and the claims must be interpreted in light of the other parts of the application including the disclosure in the specification and the definitions provided therein.

Under current law, 35 U.S.C. §112, second paragraph, requires that the specification provide a description that is understood by one of skill in the art. The skilled artisan, when equipped with the present disclosure, including the definition of a "substantially in a state of no growth," the extensive art knowledge relating the desirability that the tumor cells not grow or divide once administered to a patient, as well as the extensive reduction to practice and disclosure provided by the specification as filed, would readily ascertain the meaning of the term set forth in claim 2, as amended, and would not have found the claim, or any claim depending therefrom, indefinite in any way.

For the reasons set forth above, Applicant respectfully submits that claim 2, as amended, and claims 6-8 depending therefrom , are not indefinite under 35 U.S.C. §112, second paragraph. Therefore, Applicant respectfully requests reconsideration and withdrawal of the

Examiner's rejection of claims 2, and 6-8, claims 1, 4 and 5, having been canceled herein in accordance with the species elections made in this application.

Rejection of Claims 1, 2, and 4-8, under 35 U.S.C. § 103(a)

Claims 1, 2, and 4-8, stand rejected under 35 U.S.C. § 103(a) as being, in the Examiner's view, unpatentable over Hoover et al. (1985, Cancer 55:1236-1243), in view of the '551 patent to Berd, *supra*, both discussed previously elsewhere herein. Applicant respectfully submits that the combination of Hoover et al. and the '551 patent does not render claims 2, and 6-8, as amended, *prima facie* obvious under 35 U.S.C. § 103(a), for the following reasons.

The three-prong test which must be met for a reference or a combination of references to establish a *prima facie* case of obviousness has not been satisfied in the instant matter. The MPEP states, in relevant part:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. MPEP § 2142.

None of these criteria have been met here.

The Examiner contends that Hoover et al. discloses immunotherapy using irradiated colon cancer cells with BCG, and acknowledges that Hoover et al. does not teach haptenization of the cells. The Examiner also asserts that the '551 patent teaches haptenized melanoma cells, but notes that the '551 patent has nothing to do with colon carcinoma. Yet the Examiner reasons that these disparate references should be combined to arrive at the present invention. Applicant respectfully submits that the combination of these references cannot support a finding of *prima facie* obviousness under 35 U.S.C. §103(a), and avers as follows.

As pointed out by the Examiner, Hoover et al. does not teach or suggest using a hapten. Also as pointed out by the Examiner, the '551 patent does not teach or suggest treating colon carcinoma. Hoover et al. does not mention haptenization and the '551 patent is silent as to melanoma. Therefore, while the present invention, reduced to practice by Applicant, may now

seem "obvious" in its approach to haptenization of adenocarcinoma tumor cells, such assertion of obviousness is based on impermissible hindsight given that the teachings of the prior art did not teach or suggest such an approach and there was no motivation, either in the art or in the references, to combine these references. Thus, the first prong for *prima facie* obviousness is not satisfied and, since all three prongs must be satisfied, the rejection should be reconsidered and withdrawn.

Further, in light of the foregoing arguments, it is clear that there was no reasonable expectation of success in combining the references to arrive at the methods of Applicant's invention. That is, a person of ordinary skill in the art would not reasonably expect to succeed in producing an immunovaccine to colon cancer by combining the teachings of Hoover et al. with those of the '551 patent. Again, this prong of the test has not been satisfied and the rejection should be reconsidered and withdrawn.

Lastly, the combined references do not teach or suggest all the claim elements since one teaches haptenized melanoma cells and the other teaches unhaptenized colon cancer cells and, given the disparate disclosures, the two cannot be harmonized.

For the reasons discussed above, the combination of Hoover et al. with the '551 patent cannot render claims 2, and 6-8 (claims 1, 4, and 5 having been canceled), as amended, *prima facie* obvious under 35 U.S.C. § 103(a) and, therefore, the rejection should be reconsidered and withdrawn.

New claims 22-24

New claims 22-24 have been added herein. These claims are amply supported throughout the specification as filed, commencing at page 8, line 22, stating that the composition of the invention has the properties of eliciting T lymphocytes that infiltrate a tumor, an inflammatory response to the tumor and 3) a delayed-type hypersensitivity (DTH) response to the tumor. Accordingly, the addition of new claims 22-24 adds no new matter. They merely recite claims similar to those now issued in the parent application.

Revocation and Appointment of Attorney

Kindly note that Applicant have now retained the undersigned as their attorney in this application. A Revocation and Appointment of Attorney by Assignee was filed in this

application on March 1, 2004, to reflect these changes. A true and correct copy of the Revocation and Appointment filed in this application is attached hereto for the Examiner's convenience. All communication concerning this application should be addressed to the undersigned.

Summary

Applicant respectfully submits that each rejection of the Examiner to the claims of the present application has been either overcome or is now inapplicable, and that each of claims 2, 6-8 and new claims 22-24, is in condition for allowance. Reconsideration and allowance of each of these claims are respectfully requested at the earliest possible date.

Respectfully submitted,

DAVID BERD

3/3/04
(Date)

By: Louis W. Beardell, Jr.

LOUIS W. BEARDELL, JR.
Registration No. 40,506
RAQUEL M. ALVAREZ
Registration No. 45,807
MORGAN, LEWIS & BOCKIUS, L.L.P.
1701 Market Street
Philadelphia, PA 19103
Telephone: (215) 963-5000
Direct Dial: (215) 963-5067
Facsimile: (215) 963-5001
E-Mail: lbeardell@morganlewis.com
Attorneys for Applicant

LWB/RMA/cnm

Enclosures (Petition for three-month extension of time and associated fee; courtesy copy of Revocation and Appointment of Attorney)